REMARKS

In response to the Office Action mailed May 23, 2008, Applicants have amended claims 1-7. Claims 9 and 10 have been canceled and no new claims have been added. It is urged that support for all the above amendments may be found throughout the specification as originally filed, for example in original claims 9 and 10. No new matter has been added. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application. Following the amendments, claims 1-7 are currently under examination in the application. Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks.

Priority

Applicant respectfully submits that an English translation of a certified copy of JP 2002-313076 is forthcoming. Applicant maintains that the presently claimed subject matter is fully supported by the priority document JP 2002-313076, and thus, is entitled to a filing date of October 28, 2002.

Claim Rejections Under 35 U.S.C. §112, second paragraph

Claims 1-7 and 9-10 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner alleges that the goal of the method of claim 1 and the final step of claim 1 do not agree.

Applicant respectfully traverses this basis of rejection and submits that the metes and bounds of the instant claims are both clear and definite. Applicant, without acquiescence and solely to point out one aspect of the presently claimed invention, has amended claims 1-7 to recite a step of determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion

is not detected. Support for this amendment can be found throughout the specification as-filed, for example in original claim 9, and thus, does not constitute new matter.

The Examiner contends that it is unclear whether the claims are intended to be limited to a method for determining a pig's resistance to an RNA virus or a method of detecting an 11bp deletion in a swine Mx1 gene. Applicant respectfully submits that the presently amended claims are drawn to a method for determining a pig's resistance to an influenza A virus, wherein the method comprises a step of detecting an 11-bp deletion in a swine Mx1 gene exon, wherein the deletion is from positions 2064 to 2074 in the nucleotide sequence of SEQ ID NO: 1 and determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected.

Applicant submits that one having ordinary skill in the art would readily appreciate that the goal of the presently claimed methods agrees with the recited steps and that the metes and bounds of the instant claims are clearly defined. Reconsideration and withdrawal of this basis of rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §112, first paragraph, enablement

Claims 1-7 and 9-10 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the enablement requirement. Specifically, the Examiner contends that the claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected to make and/or use the invention.

Applicant respectfully traverses this basis of rejection and submits that the instant specification amply enables the skilled artisan to practice the entire breadth of the presently claimed invention without undue experimentation. Nevertheless, Applicant has amended claims 1-7. Support for these amendments can be found throughout the specification as filed, for example in original claims 9 and 10, and thus, do not constitute new matter.

Applicant submits that "[t]he fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." *In re Certain*

Limited-Charge Cell Culture Microcarriers, 221 USPQ 1165, 1174 (Int'l Trade Comm'n 1983), *aff 'd. subnom., Massachusetts Institute of Technology v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985). See also *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976).

The following factors (so called "Wands factors") are discussed in detail below in connection with the claimed subject matter of the present application: the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The Breadth of the Claims

The Examiner alleges that the claims are extremely broad. Specifically, the Examiner contends that the claims are drawn to a method for determining a pig's resistance to an RNA virus. The Examiner contends that the claims are broad because they encompass any breed of pig; any RNA virus; and do not state whether it is the presence or absence of the deletion that is indicative of resistance to the RNA virus.

Applicant respectfully disagrees and points out that the claims have been amended to recite wherein the virus is an influenza A virus and to recite a step of determining, wherein the presence of the 11 bp deletion in a swine Mx1 gene indicates that the subject pig is susceptible to influenza A viral infection. The art has demonstrated that the 11 bp deletion in the Mx1 gene is present at high frequency in Landrace and Hampshire breeds and at a lower frequency in Duroc and Berkshire breeds (see Morozumi et al. Biochemical Genetics 8/2001, page 259, lines 20-21). Furthermore, given the state of the art in molecular biology and the level of skill in the art, it would have been trivial to identify the presence of the 11 bp deletion in any other breed of pig. For example, Morozumi et al. describe cloning the Mx1 genes from 15 breeds of swine and analyzing them for mutations, including the 11 bp deletion. Applicant respectfully submits that the instant claims do not require that a breed of pig have the 11 bp

deletion, but rather, the instant claims are directed a method for determining a pig's resistance to an influenza A virus, wherein the method comprises detecting the presence or absence of the deletion and determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected.

The Examiner further contends that the term "resistance" is broad because it encompasses complete and partial resistance. Applicants respectfully submit that the term "resistance" is used with its ordinary and customary meaning. Applicants note that "claim terms are presumed to have the ordinary and customary meanings attributed to them by those of ordinary skill in the art." *Sunrace Roots Enter. Co. v. SRAM Corp.*, 336 F.3d 1298, 1302, 67 USPQ2d 1438, 1441 (Fed. Cir. 2003); *Brookhill-Wilk 1, LLC v. Intuitive Surgical, Inc.*, 334 F.3d 1294, 1298, 67 USPQ2d 1132, 1136 (Fed. Cir. 2003) ("In the absence of an express intent to impart a novel meaning to the claim terms, the words are presumed to take on the ordinary and customary meanings attributed to them by those of ordinary skill in the art.")

Accordingly Applicants submit that the scope of the instant claims is not broad, but is fully supported by the as-filed specification and what was known in the art at the time of filing the instant application. Moreover, one having ordinary skill in the art would be able to practice the entire breadth of the presently claimed invention in view of the guidance provided in as-filed specification without undue experimentation.

The Nature of the Invention

The Examiner has alleged that the invention is in a field that the courts have deemed "the unpredictable arts such as chemistry and biology". Applicant disputes this allegation. Although there have been several court rulings that have defined biology as an unpredictable art, all of these rulings were in reference to specific technologies. For example, prior to the advent of genetic engineering techniques, the courts routinely held that it was not possible to, through written description alone, provide enablement for the "making" of a genetically modified organism. Furthermore, Applicants submit that the case law the Examiner has mis-cited in the instant Action speaks to genetically modified organisms and is not applicable

to the presently claimed invention. Applicants respectfully submit that the presently claimed invention does not claim genetically modified organisms, but rather a method for determining a pig's resistance to an influenza A virus comprising detecting an 11-bp deletion in a swine Mx1 gene exon and determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected.

The present invention is predicted, in part, on the demonstration in the as-filed specification, which provides evidence in the form of *in vitro* cell culture experiments, clearly demonstrating that 3T3 cells transfected with an swine Mx1 gene construct harboring an 11 bp deletion are unable to suppress an influenza viral infection compared to 3T3 cells transfected with a wild-type swine Mx1 gene construct. Thus, one having ordinary skill in the art would reasonably predict that detection of the Mx1 11 bp deletion in a swine Mx1 gene would result in decreased resistance and/or increased susceptibility to influenza A viral infection.

The State of the Prior Art

The Examiner does not explicitly address the state of the prior art but generally asserts that the state of the art is unpredictable. Applicant respectfully submits that the instant claims are drawn to a method of determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected.

As discussed above, although the prior art does not teach or suggest that swine having an Mx1 gene with an 11 bp deletion have decreased resistance to influenza A virus, Morozumi et al., *Biochemical Genetics* 8/2001, page 259, lines 20-21 (Morozumi et al., 2001) have demonstrated that the 11 bp deletion in the Mx1 gene is present at high frequency in Landrace and Hampshire breeds and at a lower frequency in Duroc and Berkshire breeds.

Thus, Applicant submits that one having ordinary skill in the art in view of the as-filed specification and the knowledge available in the prior art would be able to practice a method for determining a pig's resistance to an influenza A virus comprising detecting the

presence or absence or the 11 bp deletion in an Mx1 gene exon in any breed of swine without undue experimentation.

The Level of Ordinary Skill in the Art

The Examiner correctly notes that the level of skill in the art of molecular biology is high. Applicant submits that the skilled artisan is likely a Ph.D. level molecular biologist and/or virologist. Thus, the level of one having ordinary skill in the art is high in both disciplines, and as such, and, in view of the guidance provided by the as-filed specification, the skilled artisan would be expected to practice the full-scope of the presently claimed invention without undue experimentation.

The Level of Predictability in the Art

The Examiner alleges that there is a high degree of unpredictablility in the art and that the skilled artisan would have to engage in undue experimentation in order to practice the presently claimed invention.

The Examiner alleges that it is highly unpredictable as to whether the results obtained in Landrace pigs could be extrapolated to other breeds of pigs. Further, the Examiner alleges that knowledge that mutations in a gene occur in one breed (i.e., Landrace pigs) does not allow one to conclude that this gene and mutations in this gene will also occur in other breeds and will be associated with resistance to RNA viruses. Yet, the Examiner has failed to identify a single example, wherein an Mx1 gene from swine, mouse, or man does not provide resistance to influenza A.

Applicant submits that Morozumi et al. have demonstrated that the 11 bp deletion in the Mx1 gene is present at high frequency in Landrace and Hampshire breeds and at a lower frequency in Duroc and Berkshire breeds. Moreover, Applicant has presented *in vitro* data supporting that an 11bp deletion in a swine Mx1 gene fails to provide resistance against influenza A virus, whereas the wild type Mx1 gene suppresses influenza A.

Thus, Applicant submits that one having ordinary skill in the art would find it straightforward to test any breed of swine for the claimed 11 bp deletion in a swine Mx1 gene

using established molecular biology techniques. Moreover, the skilled artisan would be able to clone and test the function of a given Mx1 gene using Applicant's cell culture assay without undue experimentation.

Direction Provided by the Inventor

One having ordinary skill in the art would conclude that the as-filed specification provides ample guidance in practicing the full breadth of the presently claimed invention without undue experimentation. Applicant has described the nature of the 11 bp deletion as lacking nucleotides 2064 to 2074 of a Landrace pig Mx1 gene. However, Morozumi et al. have demonstrated that the very same deletion occurs at high frequency in Landrace and Hampshire breeds and at a lower frequency in Duroc and Berkshire breeds. Thus, the skilled artisan would be expected to be able to clone an Mx1 gene from any breed of swine, and analyze said gene for the presently claimed deletion. Such would merely be considered routine experimentation, as demonstrated by Morozumi et al., who carried out this process on 15 breeds of swine.

Applicant has thoroughly described how to make and use (i.e., clone and express) Mx1 protein as well how to determine whether an Mx1 gene from a breed other than Landrace pigs would be able to provide protection against influenza A virus. The techniques of gene cloning are routine and apply similarly to any breed of swine (Morozumi et al.). Furthermore, Applicant has successfully demonstrated a modular 3T3 cell culture assay system, which would merely require substitution of the Mx1 gene to be assayed within the established protocol. The assay system was shown to be effective in demonstrating that a swine Mx1 gene having the claimed 11 bp deletion is susceptible to, and, has lost the ability to suppress influenza A virus, while the wild type Mx1 gene provides resistance to influenza A virus.

Thus, Applicant submits that one having skill in the art would be able to test for the presence of the claimed 11 bp deletion in a swine Mx1 gene and evaluate the ability of any swine Mx1 gene (with or without a deletion) to provide resistance against influenza A virus using Applicant's cell culture assay. Given the detailed guidance present in the as-filed specification, such experimental would be considered routine and not undue.

Existence of Working Examples

The Examiner alleges that the specification does not demonstrate that the 11 bp deletion occurs in any other breeds of swine and that the teachings in the specification are limited to the Landrace breed. Applicant strongly disagrees and submits that the as-filed specification has provide substantial detail in how to make and use the invention as claimed, and that the skilled artisan would not be required to engage in undue experimentation in order to practice the presently claimed invention.

The Examiner further alleges that the specification does not demonstrate that Landrace pigs without the 11 bp deletion can suppress any type of RNA virus and that the teachings in the specification are limited to influenza A virus. As acknowledged by the Examiner, the specification teaches an association between the presence of an 11 bp deletion of the Mx1 gene of a Landrace pig and reduced resistance (or increased susceptibility) to influenza A virus compared to a wild-type swine Mx1 gene (see page 8 of the present Action). Applicants submit and the Examiner has acknowledged that the as-filed specification teaches that an Mx1 gene having an 11 bp deletion has completely lost the ability to suppress virus propagation.

However, the Examiner concludes that the absence of the 11 bp deletion does not appear to make the sample resistant to the virus, but rather, the deletion only appears to suppress the virus for a longer amount of time. As described in the as-filed specification on page 19, lines 25-26, no further increase in the viral propagation was recorded in the wild-type Mx1 expressing 3T3 cells after 48 hours; thus, indicating viral propagation was suppressed (see Fig. 3). Applicant's data clearly supports that influenza A virus was suppressed by a swine Mx1 gene lacking the 11 bp deletion, but not in 3T3 cells having a swine Mx1 gene comprising the 11 bp deletion.

As mentioned above, the art has shown that the 11 bp deletion in swine Mx1 gene exists in 4 of 15 breeds examined (see Morozumi et al.). Thus, it would be considered merely routine to test any breed of swine for the presence of the presently claimed 11 bp deletion in a swine Mx1 gene. Moreover, Applicant provides a modular framework of examples for the detection of the 11 bp deletion in a swine Mx1 gene using PCR (Example 7), the cloning of an Mx1 gene (Example 1), preparation of an Mx1 gene construct (Example 2), preparing Mx1 gene

transformants (Example 3), preparing influenza virus particles (Example 4), and infecting the Mx1 transformants with influenza virus and assaying the ability of an Mx1 protein to provide resistance against an influenza virus (Example 5). Thus, one having ordinary skill in the art would merely need to substitute the Mx1 gene of interest in place of those exemplified in the as-filed specification in order to practice the presently claimed invention.

Thus, Applicant submits that the teachings and examples provided in the as-filed specification amply support the ability of the skilled artisan to practice a method for determining a pig's resistance to an influenza A virus, wherein the method comprises detecting the presence or absence of the deletion and determining that a subject pig is susceptible to an influenza A virus when the 11-base deletion is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected.

However, Applicant respectfully submits that "[c]ompliance with the enablement requirement of 35 U.S.C. 112, first paragraph, does not turn on whether an example is disclosed. An example may be "working" or "prophetic." A working example is based on work actually performed. A prophetic example describes an embodiment of the invention based on predicted results rather than work actually conducted or results actually achieved. An applicant need not have actually reduced the invention to practice prior to filing." In *Gould v. Quigg*, 822 F.2d 1074, 1078, 3 USPQ 2d 1302, 1304 (Fed. Cir. 1987). Furthermore the courts have held that "[t]he mere fact that something has not previously been done clearly is not, in itself, a sufficient basis for rejecting all applications purporting to disclose how to do it." 822 F.2d at 1078, 3 USPQ2d at 1304 (quoting *In re Chilowsky*, 229 F.2d 457, 461, 108 USPQ 321, 325 (CCPA 1956)).

Quantity of Experimentation Needed

The Examiner alleges that given the alleged lack of disclosure in the specification and in the prior art and the level unpredictability in the art, that the skilled artisan would need to engage in undue experimentation to make and use the invention as broadly claimed. Applicant submits that the skilled artisan would merely engage in routine, and not overly complex, experimentation in order to practice the full scope of the presently claimed invention.

For example, the methods described by Morozumi et al., demonstrate that the skilled artisan is able to assay Mx1 genes from many different breeds (e.g., 15) of swine without undue experimentation. Furthermore, Applicant provides detailed modular examples in the as-filed specification, which would, in fact, allow the skilled artisan to routinely substitute the Mx1 gene to be tested in the protocol of Applicant, and practice a method of determining a pig's resistance to influenza a virus. One having ordinary skill in the pertinent art has a high level of skill in molecular biology and virology, and thus, would carryout the presently claimed methods using routine experimentation and the ample guidance provided in the as-filed specification.

Accordingly, Applicant submits that one having ordinary skill in the art would reasonable conclude that the as-specification enables one to practice the full scope of the presently claimed invention without undue experimentation, thus, comporting with the enablement requirement of 35 U.S.C. §112, first paragraph. Reconsideration and withdrawal of this basis for rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §102(a)

Claims 1-2 stand rejected under 35 U.S.C. §102(a), as allegedly being anticipated by Asano et al. (J. Vet. Med. Sci. 12/2002). Specifically, the Examiner contends that Asano et al. teaches that Mx1 cDNA derived from PK(15) cells has the 11 bp deletion claimed by Applicant, and further teaches a method that comprises the step of detecting an 11bp deletion in a swine Mx1 gene exon.

Applicant respectfully traverses this basis of rejection and submits that Asano et al. fails to anticipate the presently claimed invention because it does not teach each and every element of the claims. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicant has amended claims 1-2 to include a step of determining that a subject pig is susceptible to an influenza A virus when the 11 bp deletion (i.e., 2064-2074 of SEQ ID

NO:1) is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected. Asano et al. fails to teach such a step or wherein the presence of the 11 bp deletion is associated with resistance to an influenza A virus. In contrast, Asano et al. teaches that there is no significant difference in the protection afforded against VSV infection by Mx1 genes amplified from PK(15) cells or LLC-PK1 cells.

Applicant notes that the basis for the amendment to claims 1-2 can be found in previous claims 9 and 10, which were not rejected as allegedly being anticipated by Asano et al. Thus, as the Examiner has acknowledged that Asano et al. fails to teach a step of determining that a subject pig is susceptible to an influenza A virus as presently claimed in claims 1-2, Asano et al. fail to anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §102(b)

Claims 1-4 stand rejected under 35 U.S.C. §102(b), as allegedly being anticipated by Morozumi et al. (Biochemical Genetics 8/2001). Specifically, the Examiner contends that Morozumi et al. describes performing PCR-RFLP on genomic DNA of 341 pigs from 15 different breeds and finding three different polymorphisms, one of which is the 11 bp deletion described by Applicant. Therefore, the Examiner concludes that Morozumi et al. teach detecting an 11 bp deletion in a swine Mx1 gene exon, wherein the deletion is from positions 2064 to 2074 of SEQ ID NO: 1.

Applicant respectfully traverses this basis of rejection and submits that Morozumi et al. fails to anticipate the presently claimed invention because it does not teach each and every element of the claims. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Applicant has amended claims 1-4 to include a step of determining that a subject pig is susceptible to an influenza A virus when the 11 bp deletion (i.e., 2064-2074 of SEQ ID NO:1) is detected or the subject pig is resistant to the influenza A virus when the deletion is not

detected. Morozumi et al. fails to teach such a step or wherein the presence of the 11 bp deletion is associated with resistance to an influenza A virus. In contrast, Morozumi et al. merely teaches that the 11 bp deletion in the Mx1 gene is present at high frequency in Landrace and Hampshire breeds and at a lower frequency in Duroc and Berkshire breeds (see Morozumi et al., page 259, lines 20-21).

Applicant notes that the basis for the amendment to claims 1-4 can be found in previous claims 9 and 10, which were not rejected as allegedly being anticipated by Morozumi et al. Thus, as the Examiner has acknowledged that Morozumi et al. fails to teach a step of determining that a subject pig is susceptible to an influenza A virus as presently claimed in claims 1-4, Morozumi et al. fails to anticipate the presently claimed invention. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §103(a), First Rejection

Claims 3-4 stand rejected under 35 U.S.C. §103(a), as allegedly being unpatentable over Asano et al. (J. Vet. Med. Sci. 12/2002) in view of Morozumi et al. (Biochemical Genetics 8/2001). Specifically, the Examiner contends that Asano et al. teaches that Mx1 cDNA derived from PK(15) cells has the 11 bp deletion claimed by Applicant, and further teaches a method that comprises the step of detecting an 11 bp deletion in a swine Mx1 gene exon. The Examiner asserts that Asano et al. fails to teach a method comprising preparing a DNA sample from a pig; optionally, amplifying the DNA region that comprises positions 2064-2074 of SEQ ID NO: 1 (claim 4); digesting the DNA with a restriction enzyme; separating the fragments based on size; and comparing the sizes of detected fragments. However, the Examiner alleges that Morozumi et al. teach these missing limitations. Therefore, the Examiner concludes that it would have been obvious to one having ordinary skill in the art at the time of the invention to substitute the deletion detection method of Asano et al. for the deletion detection method of Morozumi et al. because the substitution would have yielded predictable results.

Applicant respectfully traverses this basis of rejection and submits that the Examiner has failed to establish a *prima facie* case of obviousness against the presently claimed invention because Asano et al. or Morozumi et al., either alone or in combination fails to teach or

suggest each and every limitation of the claims. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Thus, Applicant submits that one having ordinary skill in the art would not have found it obvious to combine the references as suggested by the Examiner and arrive at the presently claimed invention.

As explained above, Applicant has amended claims 3-4 to include a step of determining that a subject pig is susceptible to an influenza A virus when the 11 bp deletion (i.e., 2064-2074 of SEQ ID NO:1) is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected. Both Asano et al. and Morozumi et al. fail to teach or suggest such a step or wherein the presence of the 11 bp deletion is associated with resistance to an influenza A virus.

Applicant reiterates that the basis for the amendment to claims 3-4 can be found in previous claims 9 and 10, which were not rejected as allegedly being unpatentable over Asano et al. in view of Morozumi et al. Thus, as the Examiner has acknowledged that both Asano et al. and Morozumi et al. fail to teach a step of determining that a subject pig is susceptible to an influenza A virus as presently claimed in claims 3-4, these references either alone or in combination fail to establish a *prima facie* case of obviousness against the presently claimed invention because they do not teach or suggest each and every limitation of the instant claims. Reconsideration and withdrawal of the rejection is respectfully requested.

Claim Rejections Under 35 U.S.C. §103(a), Second and Third Rejections

Claims 5-7 stand rejected under 35 U.S.C. §103(a), as allegedly being anticipated by Asano et al. (J. Vet. Med. Sci. 12/2002) in view of Singh (U.S. Patent No. 6,322,980). Specifically, the Examiner contends that Asano et al. teaches that Mx1 cDNA derived from PK(15) cells has the 11 bp deletion claimed by Applicant, and further teaches a method that comprises the step of detecting an 11bp deletion in a swine Mx1 gene exon, but fails to teach a method comprising preparing a DNA sample from a pig; amplifying the DNA region that comprises positions 2064-2074 of SEQ ID NO: 1; **and** dissociating the amplified DNA into single strands, separating the dissociated single-stranded DNAs on a non-denaturing gel, and

comparing the gel mobility of the fractionated single-stranded DNAs with that of a control (claim 5) **or** determining the molecular weight of the amplified DNA by mass spectrometry and comparing the molecular weight determined in step of the amplified DNA with that of a control (claim 6) **or** preparing a substrate with an immobilized nucleotide probe, contacting the amplified DNA with the substrate having an immobilized nucleotide probe, determining the intensity of hybridization between the DNA and the nucleotide probe immobilized on the substrate, and comparing the intensity determined of hybridization with that of a control (claim 7). The Examiner alleges that Singh et al. disclose multiple methods for detecting the presence of nucleic acid variants. Therefore, the Examiner concludes that one having ordinary skill in the art would have found it obvious at the time of the invention to substitute the deletion detection method of Asano et al. for any of the deletion detection methods of Singh because the substitution would have yielded predictable results.

Claims 5-7 stand rejected under 35 U.S.C. §103(a), as allegedly being anticipated by Morozumi et al. (Biochemical Genetics 8/2001) in view of Singh (U.S. Patent No. 6,322,980). Specifically, the Examiner contends that Morozumi et al. described performing PCR-RFLP on genomic DNA of 341 pigs from 15 different breeds and finding three different polymorphisms, one of which is the 11 bp deletion described by Applicant. Therefore, the Examiner concludes that Morozumi et al. teach detecting an 11 bp deletion in a swine Mx1 gene exon, wherein the deletion is from positions 2064 to 2074 of SEQ ID NO: 1, but fails to teach a method comprising preparing a DNA sample from a pig; amplifying the DNA region that comprises positions 2064-2074 of SEQ ID NO: 1; **and** dissociating the amplified DNA into single strands, separating the dissociated single-stranded DNAs on a non-denaturing gel, and comparing the gel mobility of the fractionated single-stranded DNAs with that of a control (claim 5) **or** determining the molecular weight of the amplified DNA by mass spectrometry and comparing the molecular weight determined in step of the amplified DNA with that of a control (claim 6) **or** preparing a substrate with an immobilized nucleotide probe, contacting the amplified DNA with the substrate having an immobilized nucleotide probe, determining the intensity of hybridization between the DNA and the nucleotide probe immobilized on the substrate, and comparing the intensity determined

of hybridization with that of a control (claim 7). The Examiner alleges that Singh et al. disclose multiple methods for detecting the presence of nucleic acid variants. Therefore, the Examiner concludes that one having ordinary skill in the art would have found it obvious at the time of the invention to substitute the deletion detection method of Morozumi et al. for any of the deletion detection methods of Singh because the substitution would have yielded predictable results.

Applicant respectfully traverses these bases for rejection and submits that the Examiner has failed to establish a *prima facie* case of obviousness against the presently claimed invention because Asano et al. or Morozumi et al., either alone or in combination with Singh fails to teach or suggest each and every limitation of the claims. To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Thus, Applicant submits that one having ordinary skill in the art would not have found it obvious to combine the references as suggested by the Examiner and arrive at the presently claimed invention.

As explained above, Applicant has amended claims 5-7 to include a step of determining that a subject pig is susceptible to an influenza A virus when the 11 bp deletion (i.e., 2064-2074 of SEQ ID NO:1) is detected or the subject pig is resistant to the influenza A virus when the deletion is not detected. Both Asano et al. and Morozumi et al. fail to teach or suggest such a step or wherein the presence of the 11 bp deletion is associated with resistance to an influenza A virus. Singh is completely silent with regard a step of determining that a subject pig is susceptible to an influenza A virus, and thus, fails to remedy the deficiencies of either Asano et al. or Morozumi et al.

Furthermore, Singh teaches methods for detecting single nucleotide polymorphisms and is completely silent with regard to detecting amplicons or DNA fragments based on the presence of a deletion. Clearly, the Examiner has violated one of the basic tenets in patent law in applying §103, in that the references must be viewed without the benefit of hindsight vision afforded by the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed.Cir.1983).

Applicant submits that the basis for the amendment to claims 5-7 can be found in previous claims 9 and 10, which were not rejected as allegedly being unpatentable over Asano et al. or Morozumi et al. in view of Singh. Thus, as the Examiner has acknowledged that both Asano et al. or Morozumi et al. in combination with Singh fail to teach a step of determining that a subject pig is susceptible to an influenza A virus as presently claimed in claims 5-7, these references either alone or in combination fail to establish a *prima facie* case of obviousness against the presently claimed invention because they do not teach or suggest each and every limitation of the instant claims. Reconsideration and withdrawal of the rejection is respectfully requested.

The Director is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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